Dr. Neal D. Barnard
Physicians' Committee for Responsible Medicine
5100 Wisconsin Ave., NW, Suite 400
Washington, D.C. 20016

Dear Dr. Barnard:

As promised at our October 17 meeting and again in Steve Johnson's October 30 letter to you, I would like to share with you specific information on the $500,000 that the Agency has placed into an Interagency Agreement with the National Institute of Environmental Health Sciences (NIEHS) to support activities related to the development and validation of non-animal test method alternatives. The enclosed one-pager outlines how these resources are being utilized. As you are aware, the National Toxicology Program (NTP) Interagency Center for the Validation of Alternative Methods at NIEHS has the lead for the Federal government for these activities.

In addition, OPPTS is co-sponsoring a workshop on February 19-21, 2002, at the NIH Natcher Center in Washington, D.C., on implementation of the revised acute oral toxicity tests. The three alternative methods – fixed dose, acute toxic class and up-and-down – reduce and help to refine animal usage compared with the traditional OECD 401 test method. An in vitro screen for acute systemic toxicity will be presented as one means of picking the starting dose for in vivo testing and further animal usage. These efforts will result in the three alternatives becoming the only means of acute oral toxicity testing, as OECD 401 will be deleted. For more information contact:

I hope this information is helpful. If you need additional information or have questions related to the $500,000, please contact Dr. Bill Stokes, Director of the NTP Center, at 919-541-2384. For HPV related issues, please contact either Priscilla Flattery at 202-260-2718 or me at 202-260-3810.

Sincerely,

William H. Sanders

EPA's Commitment of $500,000 for Development and
Validation of In Vitro Test Methods

-- In accordance with EPA's October 14, 1999, letter to HPV Chemical Challenge Sponsors which outlined 10 animal welfare principles, EPA placed $500,000 into an Interagency Agreement with the National Institutes of Environmental Health Sciences to support an in vitro validation project.

-- This effort began with an October 2000 Workshop on In Vitro Methods for Assessing Acute Systemic Toxicity. Based on recommendations of participants at the Conference, efforts have begun on the use of two
in vitro basal cytotoxicity assays to predict starting doses for in vivo acute lethality assays.

–- This study involves the participation of several laboratories in the evaluation of the neutral red uptake assay using both a mouse cell line (i.e., BALB/c 3T3 fibroblasts) and a primary human cell type (i.e., normal human epithelial keratinocytes).

-- The cytotoxicity results for the 60-75 chemicals tested in these assays will be used to:

  -- standardize and optimize two in vitro cytotoxicity protocols in order to maximize intra- and inter laboratory reproducibility,

  -- determine the effectiveness of the in vitro cytotoxicity assays to estimate starting doses for in vivo acute toxicity testing,

  -- establish a high quality in vitro basal cytotoxicity database for acute toxicity. Such a database could be used to evaluate the extent that other specialized in vitro methods would further improve the accuracy of in vitro predictions of acute toxicity, and potentially lead to further reduction or replacement of animal use.

-- Laboratory testing is expected to be complete by the fall of 2002. Results will then be compiled and evaluated by an expert peer review panel in 2003.

-- Project costs beyond the $500,000 are being incurred by NIEHS to obtain and distribute the 60-75 coded chemicals for testing. The European Committee on the Validation of Alternative Methods (ECVAM) will also fund a third lab in Europe, using EU funds.

– Additional information on this effort can be obtained from the website for the NTP Interagency Center for the Validation of Alternative Methods at http://iccvam.niehs.nih.gov, or by contacting the Center Office at 919-541-2384 or by email at niceatm@niehs.nih.gov.